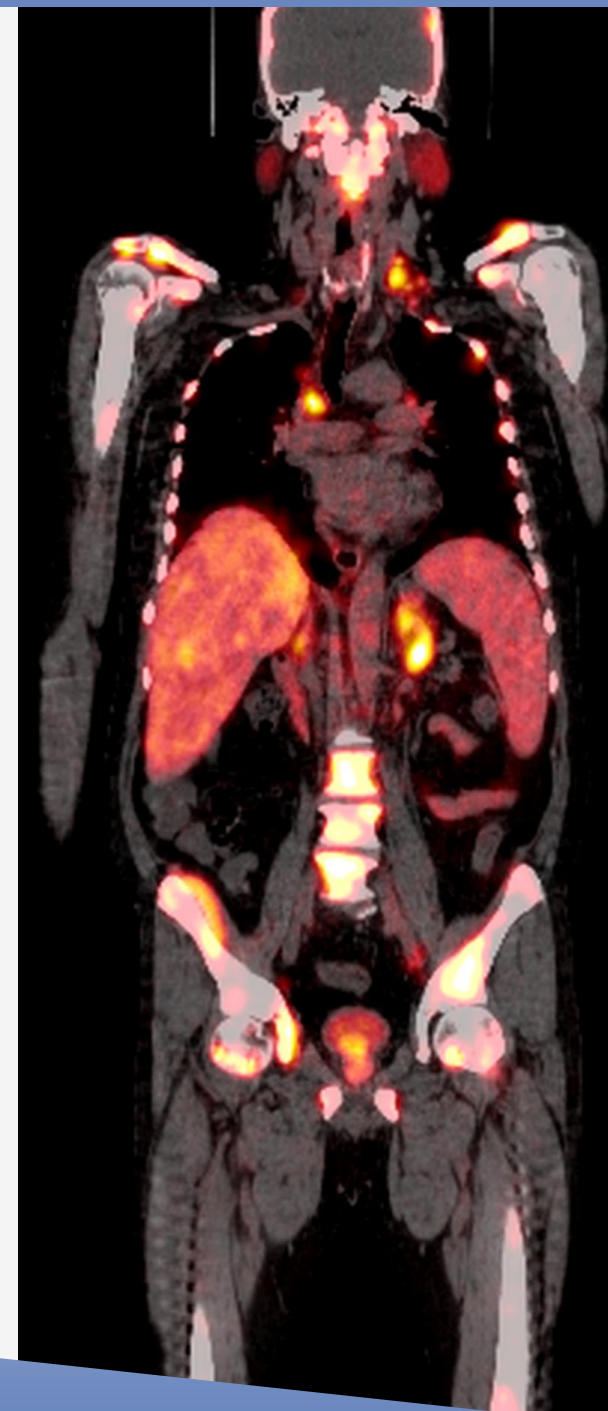




The ENHANCING Study

^{68}Ga -PSMA-PET/CT imaging in metastatic prostate cancer with anti-androgen medication: effects of castrate sensitivity versus castrate resistance

August 2019



Notices

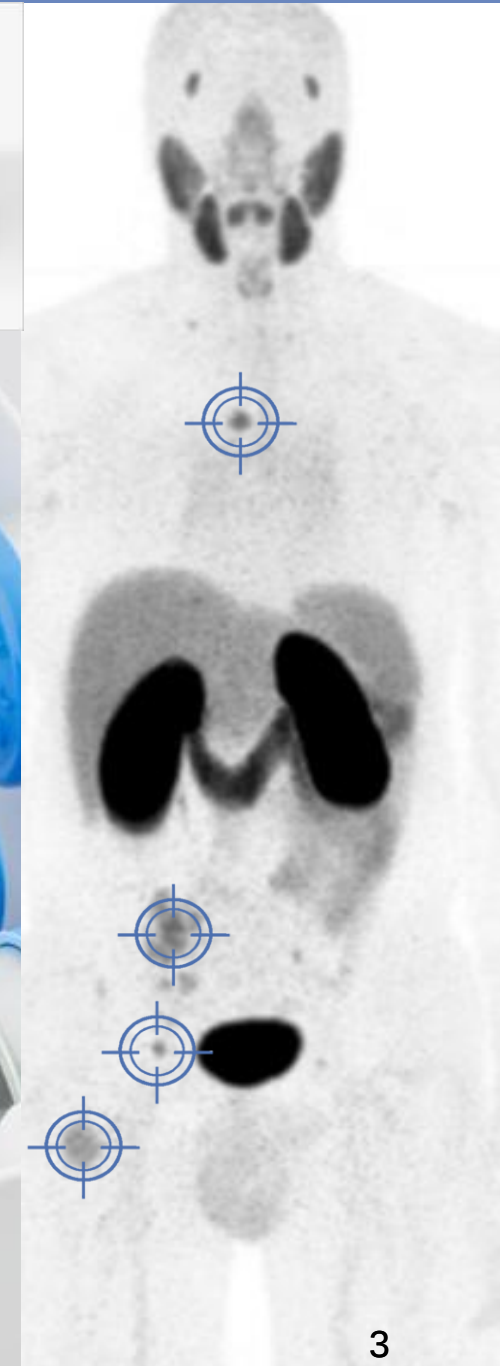
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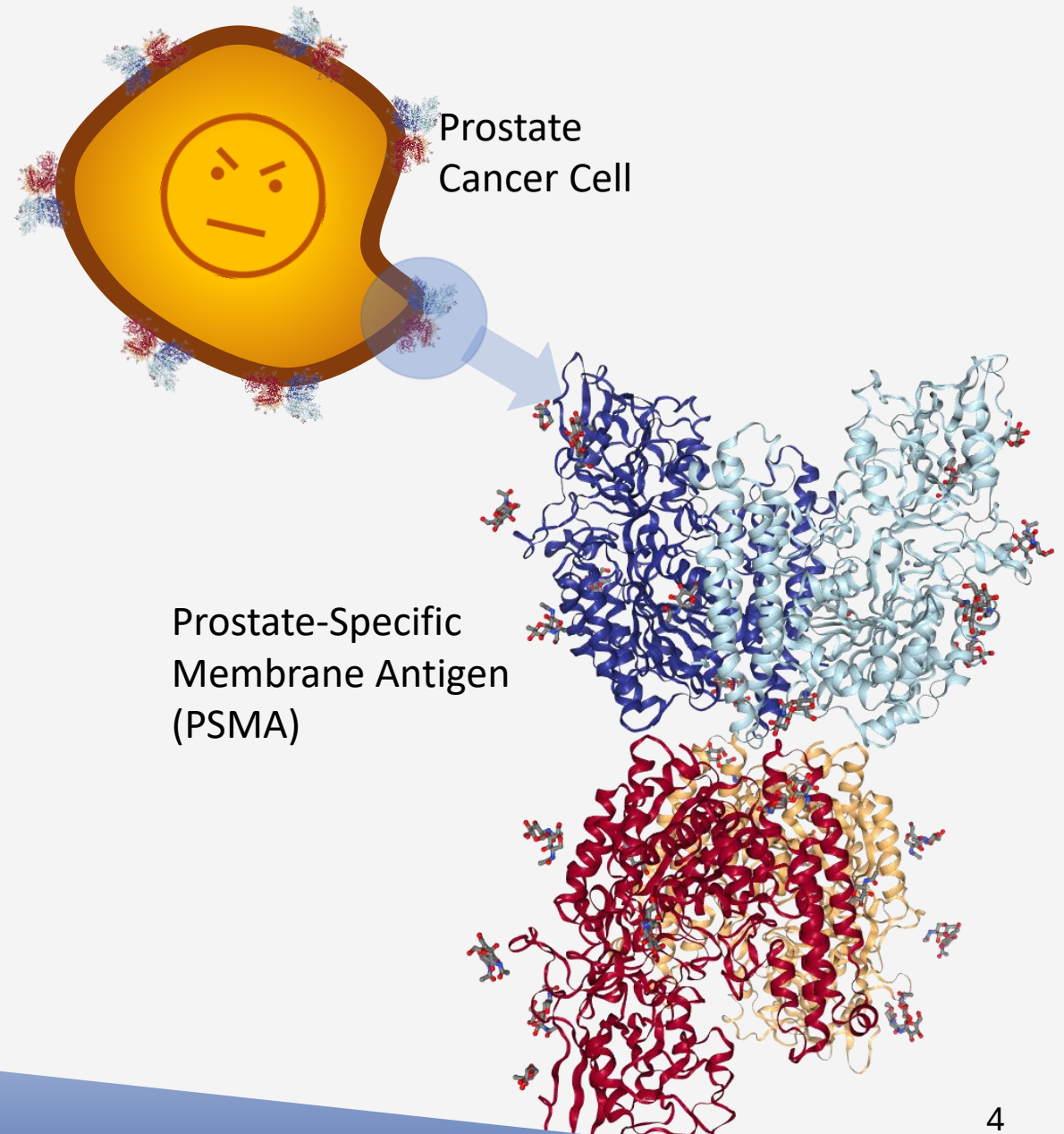
Executive Summary

- ENHANCING (enzzalutamide-enhanced imaging) is a Phase II, single center, prospective open label clinical study for men with metastatic prostate cancer (mPC)
- The aim of ENHANCING is to assess how androgen-deprivation therapy with enzalutamide (Xtandi®¹) influences the diagnostic sensitivity of TLX591-CDx (⁶⁸Ga-PSMA-11)
- The results of ENHANCING will have important implications for the diagnosis and treatment of mPC, especially for combining androgen-deprivation therapy and PSMA-targeting therapeutics (e.g. TLX591)

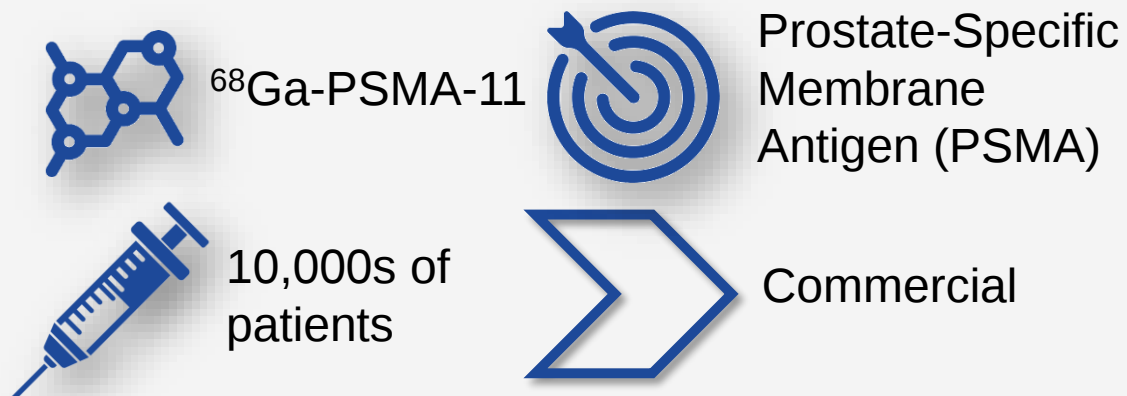


What is PSMA?

- Prostate-Specific Membrane Antigen
- A well-validated cell surface target for both diagnostic imaging and treatment of mPC
- Over-expressed in 90-95% of mPC
- Expressed by both primary and metastatic tumours
- PSMA expression is particularly elevated in poorly differentiated, metastatic, and castrate-resistant prostate cancer



TLX591-CDx (PSMA Imaging)



- TLX591-CDx is a proprietary formulation of the most popular PSMA imaging agent (PSMA-11)
- Sterile “cold kit”
 - ✓ Room temperature radiolabelling in minutes
 - ✓ “Dose on demand”
- Available in the US / EU for investigational and named-patient use



- PSMA-11 is the most widely used PSMA prostate cancer imaging agent
- Clinically validated with >150 publications
- Excellent detection of prostate cancer in a range of patient groups from high-risk pre-prostatectomy patients to metastatic disease
- Included in the European Association of Urology (EAU) guidelines for prostate cancer management



Commercialisation in Progress

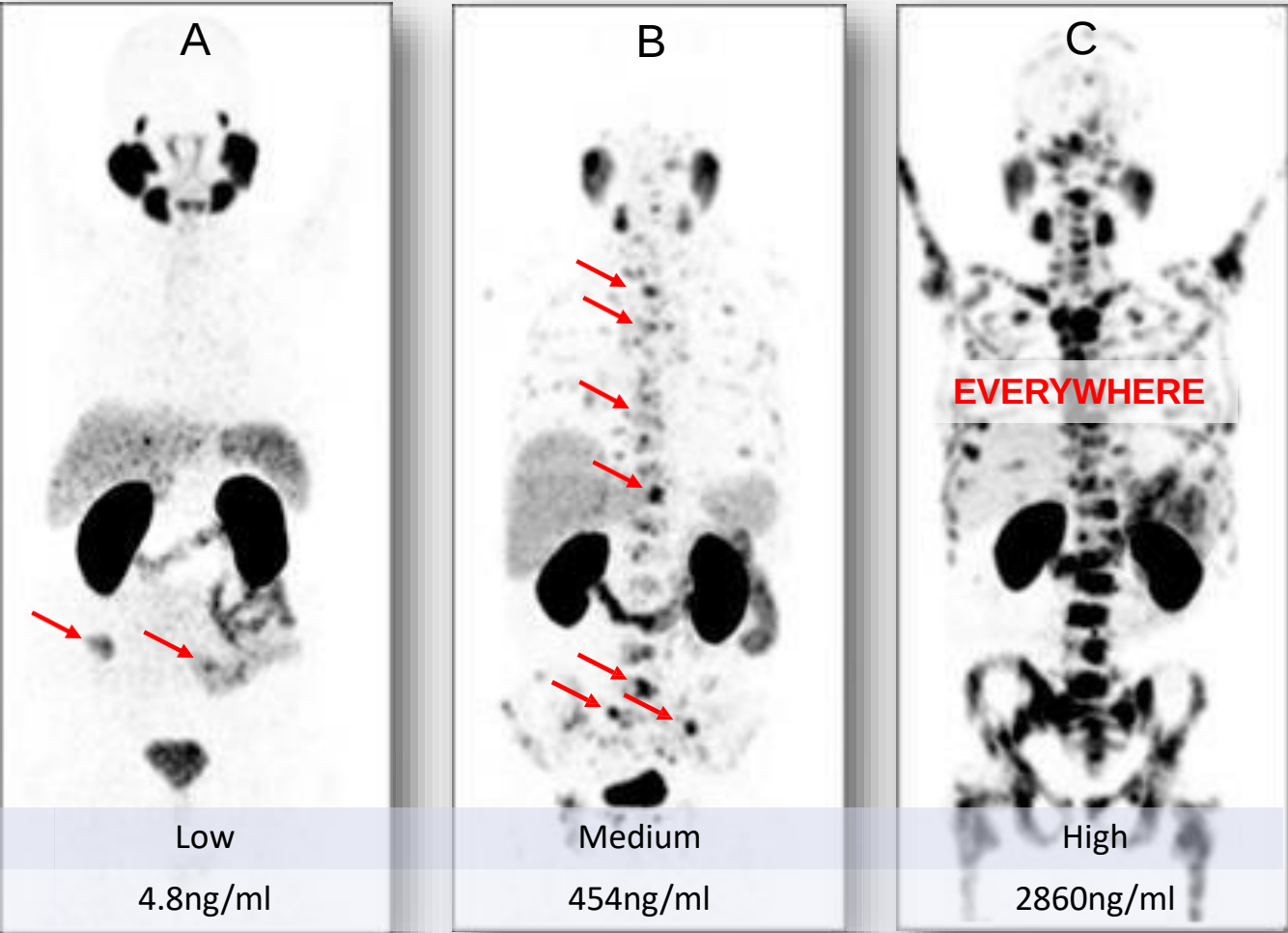
- Pre-NDA package has been presented to the FDA (24/07/19)
- Scale-up manufacturing completed (US)
- Extensive US and EU clinical data package and supporting literature
- Parallel discussions in progress with EU authorities for product approval

PSMA Imaging with PET is Sensitive, Correlates with Blood PSA

It is possible to image PSMA expression with PET imaging, even at very low blood PSA levels (= generally lower tumor burden). TLX591-CDx uses the PSMA-11 targeting peptide, one of the most widely studied PC imaging agents

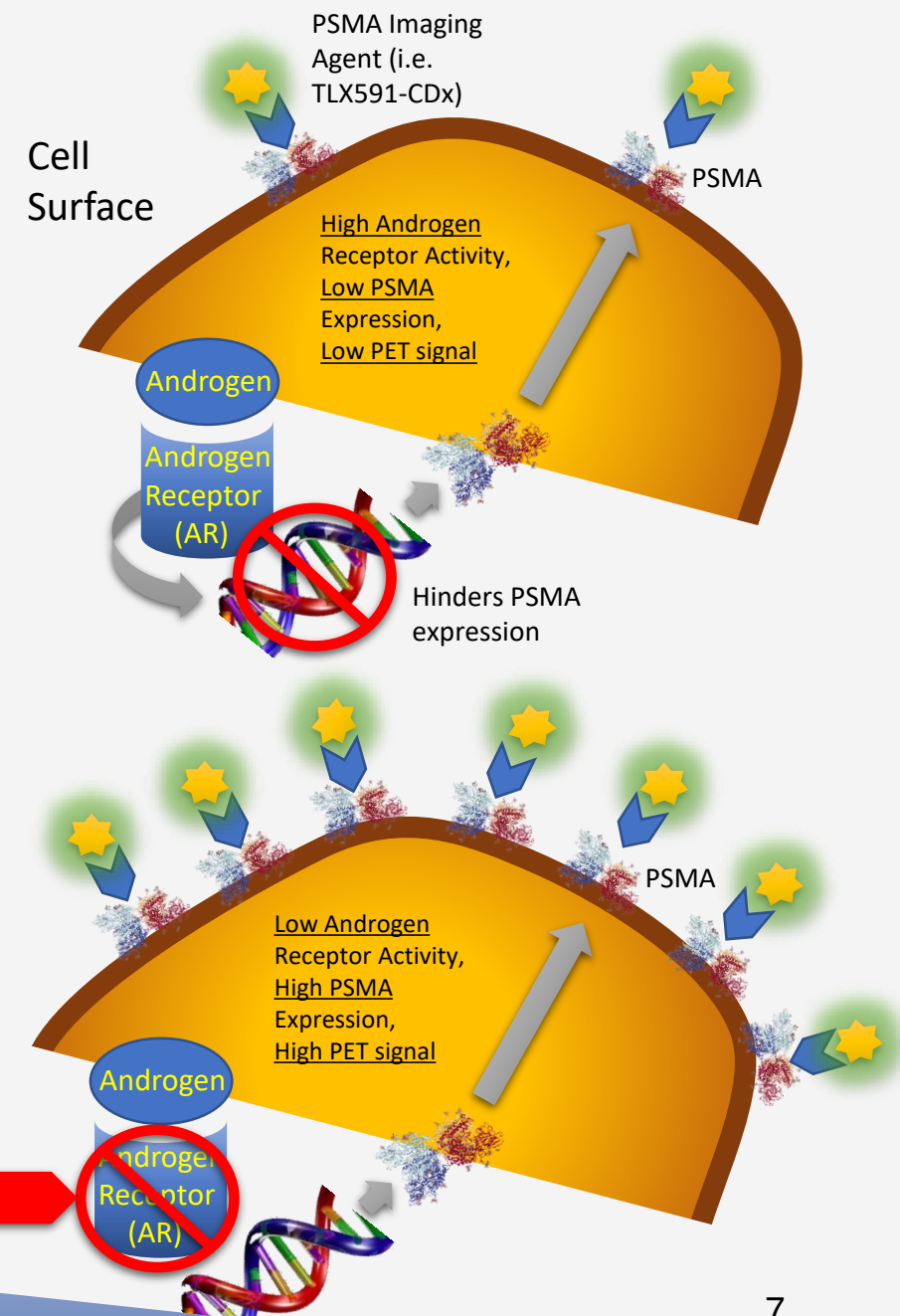
The three panels A)-C) illustrate how PSMA imaging avidity changes as a function of PSA level (from low to high PSA). All of these metastatic patients are imaged post-prostatectomy¹

A few highly vivid tumors are marked for noting (red arrows)



Androgen Deprivation Therapy and PSMA

- Androgen¹ deprivation therapy (ADT) is part of standard care for PC with a ~USD \$9Bn worldwide market
- The effect of androgen deprivation on PSMA expression is an important clinical question for the management of PC
- In pre-clinical studies, blocking the androgen pathway has been shown to increase PSMA expression²
- Limited clinical study in patients with castration-resistant PC treated with ADT suggests increased PSMA expression that is detectable with PSMA PET imaging³
- **If PSMA imaging with TLX591-CDx can confirm and quantify this effect, then the use of drugs such as enzalutamide could potentially be leveraged to further enhance the efficacy of targeted PSMA radiotherapy (i.e. TLX591) when used in combination**



ENHANCING* Study Design : Overview



Phase II, single center, prospective open label clinical trial

Patient Population A

Men with metastatic prostate cancer with demonstrated castrate sensitivity (n = 20)

Patient Population B

Men with metastatic prostate cancer with demonstrated castrate resistance (n = 20)

Imaging

⁶⁸Ga-PSMA-PET/CT

Treatment

Enzalutamide, 160 mg PO,
14 days

Imaging

⁶⁸Ga-PSMA-PET/CT

Primary outcome(s)

1. To evaluate if **diagnostic sensitivity of ⁶⁸Ga-PSMA-PET/CT imaging in patients with metastatic prostate cancer is enhanced by androgen blockade with enzalutamide**, or any **increase in number of lesions detected in an individual patient**

Key secondary outcomes

1. To compare degree of enhanced diagnostic sensitivity of ⁶⁸Ga- PSMA-PET/CT imaging in metastatic castrate-resistant prostate cancer versus metastatic castrate sensitive prostate cancer.
2. To report any incidental findings on ⁶⁸Ga-PSMA-PET/CT following androgen blockade

Summary

- Androgen deprivation therapy (ADT) is a fundamental part of prostate cancer therapy
- Blocking the effects of androgen slows the growth of prostate cancer and boosts the expression of PSMA in certain patients
- The ENHANCING study compares the enzalutamide-induced expression of PSMA in patients that are castrate sensitive and castrate resistant. This will have two important outcomes:
 1. Better understanding of how to interpret PSMA imaging in prostate cancer patients undergoing ADT therapy
 2. Provide insights into the combination use of enzalutamide (Xtandi®) with PSMA-targeting therapeutic radiopharmaceuticals (i.e. TLX591)





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